DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/28/2008 has been entered.

Claims 40-59 are pending and have been examined on the merits.

Claims 40, 44-46, 50, 54-56 have been amended.

Response to Arguments

Applicant's arguments with respect to claims 40-59 have been considered but are moot in view of the new ground(s) of rejection.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 50 is ambiguous, and thus indefinite, because it is unclear exactly what the metes and bounds of the claimed invention are. It is unclear if Applicant is intending to claim just the hydrogel produced or intends to include the extracellular matrix that is attached to the hydrogel as well as the mammal the hydrogel is applied to. For examination purposes, the claim is interpreted as being drawn only to the hydrogel as directed by the preamble of the claim and does not include the extracellular matrix or the mammal.

Applicant's claims 51-59 are ambiguous, and thus indefinite, because they are directed to both a method and a composition; therefore it is not clear what applicant is intending to claim: a hydrogel or a method of making the hydrogel. See *Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) & MPEP 2173.05(p). While the claim is indefinite, in order to provide compact prosecution, the claims will be examined as composition claims, (in a product-by-process manner, wherein the method of producing the hydrogel will be considered in so far as it affects the composition itself).

Clarification is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 51-59 are rejected under 35 U.S.C. 101 because the subject matter claimed does not fall into a single statutory class of invention, as these claims cite both a composition and a method; therefore they are directed to neither a composition or a method, but rather encompass or overlap two different statutory classes of invention. The language of 35 USC 101 prohibits overlap between two different statutory classes in a single claim as it is drafted so as to set forth the statutory classes of invention in the alternative only. See *Ex parte Lyell,* 17 USPQ2d 1551 (Bd. Pat. App. & Inter. 1990).

Amending claims 51-59 so that they are drawn to the hydrogel of claim 50 would overcome this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 40-42, 44-52, 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al (US 6,624,245) in view of Benson (Nuclear Instruments and Methods in Physics Research 2002).

Amended claim 40 is now drawn to a method of integrating a hydrogel to an extracellular matrix (ECM), comprising: a) priming an ECM by treating with a priming agent, wherein said priming comprises reacting said priming agent with said ECM to covalently bind said ECM and said priming agent, and said priming agent comprises a polysaccharide with at least one aldehyde group and at least one free radical polymerizable group; b) adding to the primed ECM a polymerizable agent and a radical photoinitiator, wherein the polymerizable agent comprises a biocompatible polymer having at least one free radical polymerizable group; and c) reacting the primed ECM and the polymerizable agent by a radical reaction to create a hydrogel covalently bound to the ECM.

Amended claim 50 is drawn to a hydrogel produced by a method comprising: a) priming an ECM by treating with a priming agent, wherein the priming agent comprises a polysaccharide with at least one aldehyde group and at least one free radical polymerizable group; b) adding to the primed ECM a polymerizable agent and a radical photoinitiator, wherein the polymerizable agent comprises a biocompatible polymer having at least one free radical polymerizable group; and c) reacting the primed ECM and the polymerizable agent by a radical reaction to create a hydrogel covalently bound

to the ECM, wherein the reacting comprising covalently binding and crosslinking of the polymerizable agent to the primed ECM.

Claims 41 and 51 include wherein the ECM is cartilage.

Claims 42 and 52 include wherein the cartilage is disposed in a mammal.

Claims 44 and 54 include wherein the priming agent has at least one free radical polymerizable group selected from a group.

Claims 45 and 55 include wherein the biocompatible polymer has at least one free radical polymerizable group selected from a group.

Claims 46 and 56 are drawn to the method and hydrogel of claims 40 and 50 respectively, and further include wherein the reacting step further comprises exposing the primed ECM and the polymerizable agent to a source of electromagnetic radiation.

Claims 47-49 and 57-59 include wherein the polymerizable agent comprises biologically active material, autologous cells, growth factor.

Wallace et al teach crosslinkable compositions that readily crosslink in situ to provide biocompatible, nonimmunogenic crosslinked biomaterials. The term "crosslinking" is defined to include the formation of covalent bonds (column 6 lines 12-15). The compositions described are delivered to the site of administration in such a way that the individual components of the composition come into contact with one another for the first time at the site of administration (the components are delivered separately and activated after application to the tissue site) (column 28 lines 3-23). This method of administration allows for a layering of the components so that the site may be "primed" first by one polymer before a second is applied. The component polymers are

taught to include hydrophilic polymers such as polysaccharides, particularly chondroitin sulfate (column 19 lines 59-67). When the polysaccharide polymer is applied before an additional polymer component, the priming of the tissue site is accomplished. Any of the hydrophilic polymers described must contain, or be modified or functionalized to contain, functional groups which enable crosslinking (column 21 lines 36-37). Reactive groups to be included in the polymer component include aldehydes and acrylates (column 15 lines 1-18). The tissue that the composition is to be applied to includes cartilage (column 9 lines 38-41) of a mammalian subject (column 32 line 26). The addition of biological agents to the crosslinked compositions includes growth factors and autogenous bone marrow (autologous cells) (column 29 line 9). "Synthetic" polymers also include semi-synthetic polymers, i.e., naturally occurring polymers, obtained from natural sources, that have been chemically modified in some way (column 8 lines 10-14). Polymer components may also react with groups on collagen molecules within the patients own tissue, providing for "biological anchoring" (covalent bonding) of the compositions with the host tissue (ECM) (column 30 lines 32-37). The use of free radical photoinitiators in conjunction with ultraviolet light in order to crosslink the polymers via a free radical mechanism is taught as well (column 23 lines 19-67).

Benson teaches that radiation induced crosslinking has allowed the tailoring of the composition and properties of hydrogels to meet numerous biomedical applications. In addition, photocrosslinking can serve to enhance the tribological properties of load bearing components of the total artificial knee and hip (page 756-Summary).

The teachings of Wallace et al would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Wallace et al include each of the claimed limitations as suitable options depending on the desired characteristics of the hydrogel and its intended use (column 34 line 17- line 25). One of ordinary skill in the art would have had a reasonable expectation of success with arriving at the claimed method and composition because Wallace et al suggest the effects that each of the modifications would have on the final hydrogel product as well.

The teachings of Benson would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice with regard to Wallace et al based on the fact that Benson teaches that radiation induced crosslinking has allowed the tailoring of the composition and properties of hydrogels to meet numerous biomedical applications. One of ordinary skill in the art would have had a reasonable expectation of success because the use of ultraviolet radiation for cross linking via a free radical reaction mechanism is suggested by Wallace et al (column 23 lines 19-67).

Therefore, the combined teachings of Wallace et al and Benson render obvious Applicant's invention as claimed.

Claims 43 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al (US 6,624,245) and Benson (Nuclear Instruments and Methods in

Physics Research 2002) as applied to claims 40-42, 44-52, 54-59 above, and further in view of Hai et al (Bioconjugate Chem. 2000).

Claims 43 and 53 are drawn to the method and hydrogel of claims 40 and 50 respectively, and further include wherein the polysaccharide is chondroitin sulfate.

Wallace et and Benson combined teach the method and hydrogel as described above, but do not specifically include wherein the polysaccharide is chondroitin sulfate with an aldehyde group.

Hai et al teach the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai et al teach that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the *in vivo* properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai et al would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice with regard to Wallace et al based on the fact that Hai et al teach the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because Wallace et al suggest the use of activated polysaccharides for the method/hydrogel as well (column 19 lines 59-67).

Therefore, the combined teachings of Wallace et al, Benson and Hai et al render obvious Applicant's invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40-59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-75 of copending Application No. 11/369,578. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application anticipate the claims of the current application since bone and osteochondral defects inherently contain extracellular matrix.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 40, 41, 42, 45-48, 50, 51, 52, 55-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 10, 15 of copending Application No. 10/962,278 in view of Hai et al (Bioconjugate Chem. 2000).

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

Claims 40, 41, 42, 45-48, 50, 51, 52, 55-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-7, 18, 22, 23 of copending Application No. 11/637,516 in view of Hai et al (Bioconjugate Chem. 2000).

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

Claims 40, 41, 42, 45-47, 49, 50, 51, 52, 55-58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53, 63, 65, 77 of copending Application No. 10/681,753 in view of Hai et al (Bioconjugate Chem. 2000).

The claims of the copending application include all the limitations of the current application except for the use of the polysaccharide chondroitin sulfate with aldehyde groups as the priming agent.

Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). Hai teaches that the modification of proteins with chondroitin-4-sulfate would add a global negative charge that has the potential to alter the in vivo properties of the proteins, and possibly increase their therapeutic utility (page 712 last paragraph).

The teachings of Hai would have rendered to one of ordinary skill in the art at the time the invention was made the claimed method/hydrogel an obvious design choice based on the fact that Hai teaches the use of chondroitin-4-sulfate containing aldehyde end groups for surface modification of a biological material (page 709 column 1). One of ordinary skill in the art would have had a reasonable expectation of success because the claimed invention is also modifying the surface of a biological material with a polysaccharide with aldehyde groups.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Laura Schuberg